MPL gene

MPL proto-oncogene, thrombopoietin receptor

Normal Function

The *MPL* gene provides instructions for making the thrombopoietin receptor protein, which promotes the growth and division (proliferation) of cells. This receptor is especially important for the proliferation of certain blood cells called megakaryocytes, which produce platelets, the cells involved in blood clotting. Research suggests that the thrombopoietin receptor may also play a role in the maintenance of hematopoietic stem cells, which are stem cells located within the bone marrow that have the potential to develop into red blood cells, white blood cells, and platelets.

The thrombopoietin receptor is turned on (activated) when a protein called thrombopoietin attaches (binds) to it. The activated thrombopoietin receptor stimulates a signaling pathway called the JAK/STAT pathway, which transmits chemical signals from outside the cell to the cell's nucleus and is important for controlling the production of blood cells.

Health Conditions Related to Genetic Changes

essential thrombocythemia

Several mutations in the *MPL* gene have been associated with a small number of cases of essential thrombocythemia, a condition characterized by an increased number of platelets in the blood. Platelets are the blood cells involved in blood clotting, and abnormal clotting (thrombosis) is common in people with essential thrombocythemia.

MPL gene mutations associated with essential thrombocythemia change a single protein building block (amino acid) in the thrombopoietin receptor protein. An inherited form of the condition, called familial essential thrombocythemia, is caused by an *MPL* gene mutation that results in the replacement of the amino acid serine with the amino acid asparagine at position 505 in the protein (written as Ser505Asn or S505N). Essential thrombocythemia that does not run in families (sporadic essential thrombocythemia) has been associated with *MPL* gene mutations that result in the replacement of the amino acid tryptophan at position 515 with another amino acid, most commonly leucine. These mutations are generally referred to as W515 mutations.

Amino acid changes at position 505 or 515 result in a thrombopoietin receptor protein that is constantly turned on (constitutively activated), which, in essential thrombocythemia, leads to the overproduction of abnormal megakaryocytes and an

increased number of platelets. Excess platelets can cause thrombosis, which leads to many signs and symptoms of essential thrombocythemia.

primary myelofibrosis

Several mutations in the *MPL* gene have been identified in some people with primary myelofibrosis. This condition is characterized by scar tissue (fibrosis) in the bone marrow, the tissue that produces blood cells.

Like essential thrombocythemia, primary myelofibrosis is associated with the *MPL* gene mutations referred to as W515 mutations. These mutations lead to a constitutively activated thrombopoietin receptor protein, which results in the overproduction of abnormal megakaryocytes. These megakaryocytes stimulate other cells to release collagen, a protein that normally provides structural support for the cells in the bone marrow but causes scar tissue formation in primary myelofibrosis. Because of the fibrosis, the bone marrow cannot produce enough normal blood cells, leading to the signs and symptoms of the condition.

It is unknown how the same gene mutations can be associated with different conditions.

other disorders

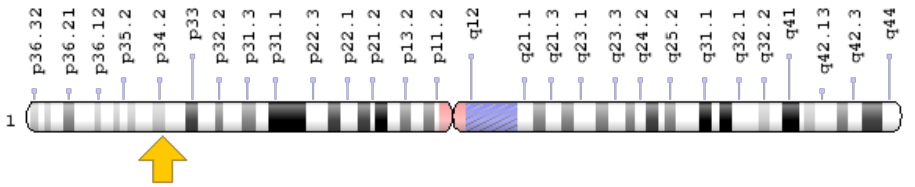
Mutations in the *MPL* gene cause a rare condition called congenital amegakaryocytic thrombocytopenia (CAMT). This condition begins in infancy and is characterized by low numbers of megakaryocytes (megakaryocytopenia) and platelets (thrombocytopenia). CAMT can lead to an impairment of bone marrow function known as bone marrow failure.

The *MPL* gene mutations involved in CAMT lead to a reduced functioning or nonfunctioning thrombopoietin receptor protein. People with no thrombopoietin receptor function have a severe form of the condition called CAMT I. People with some remaining thrombopoietin receptor function have a milder form of the condition called CAMT II.

Chromosomal Location

Cytogenetic Location: 1p34.2, which is the short (p) arm of chromosome 1 at position 34.2

Molecular Location: base pairs 43,336,875 to 43,354,464 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- C-MPL
- CD110
- MPLV
- myeloproliferative leukemia protein
- myeloproliferative leukemia virus oncogene
- proto-oncogene c-Mpl
- thrombopoietin receptor
- thrombopoietin receptor precursor
- TPO-R
- TPOR
- TPOR_HUMAN

Additional Information & Resources

Genetic Testing Registry

- GTR: Genetic tests for MPL
  https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4352%5Bgeneid%5D

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MPL%5BTIAB%5D%29+OR+%28myeloproliferative+leukemia+virus+oncogene%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D

OMIM

- MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE
  http://omim.org/entry/159530

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_MPL.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MPL%5Bgene%5D
- HGNC Gene Family: CD molecules
  http://www.genenames.org/cgi-bin/genefamilies/set/471
- HGNC Gene Family: Fibronectin type III domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/555
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7217
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4352
- UniProt
  http://www.uniprot.org/uniprot/P40238

Sources for This Summary

- Chaligné R, Tonetti C, Besancenot R, Roy L, Marty C, Mossuz P, Kiladjian JJ, Socié G, Bordessoule D, Le Bousse-Kerdilès MC, Vainchenker W, Giraudier S. New mutations of MPL in primitive myelofibrosis: only the MPL W515 mutations promote a G1/S-phase transition. Leukemia. 2008 Aug;22(8):1557-66. doi: 10.1038/leu.2008.137. Epub 2008 Jun 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18528423
- Ding J, Komatsu H, Iida S, Yano H, Kusumoto S, Inagaki A, Mori F, Ri M, Ito A, Wakita A, Ishida T, Nitta M, Ueda R. The Asn505 mutation of the c-MPL gene, which causes familial essential thrombocythemia, induces autonomous homodimerization of the c-Mpl protein due to strong amino acid polarity. Blood. 2009 Oct 8;114(15):3325-8. doi: 10.1182/blood-2008-04-149047. Epub 2009 May 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19483125

- Germeshausen M, Ballmaier M, Welte K. MPL mutations in 23 patients suffering from congenital amegakaryocytic thrombocytopenia: the type of mutation predicts the course of the disease. Hum Mutat. 2006 Mar;27(3):296.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16470591
- OMIM: MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE
  http://omim.org/entry/159530
- Pikman Y, Lee BH, Mercher T, McDowell E, Ebert BL, Gozo M, Cuker A, Wernig G, Moore S, Galinsky I, DeAngelo DJ, Clark JJ, Lee SJ, Golub TR, Wadleigh M, Gilliland DG, Levine RL. MPLW515L is a novel somatic activating mutation in myelofibrosis with myeloid metaplasia. PLoS Med. 2006 Jul;3(7):e270.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16834459
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1502153/
- Tefferi A. Novel mutations and their functional and clinical relevance in myeloproliferative neoplasms: JAK2, MPL, TET2, ASXL1, CBL, IDH and IKZF1. Leukemia. 2010 Jun;24(6):1128-38. doi: 10.1038/leu.2010.69. Epub 2010 Apr 29. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20428194
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3035972/

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Reviewed: September 2014
Published: January 24, 2017

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